MMed and DCH Lectures

Neonatology II: Neonatal Infections

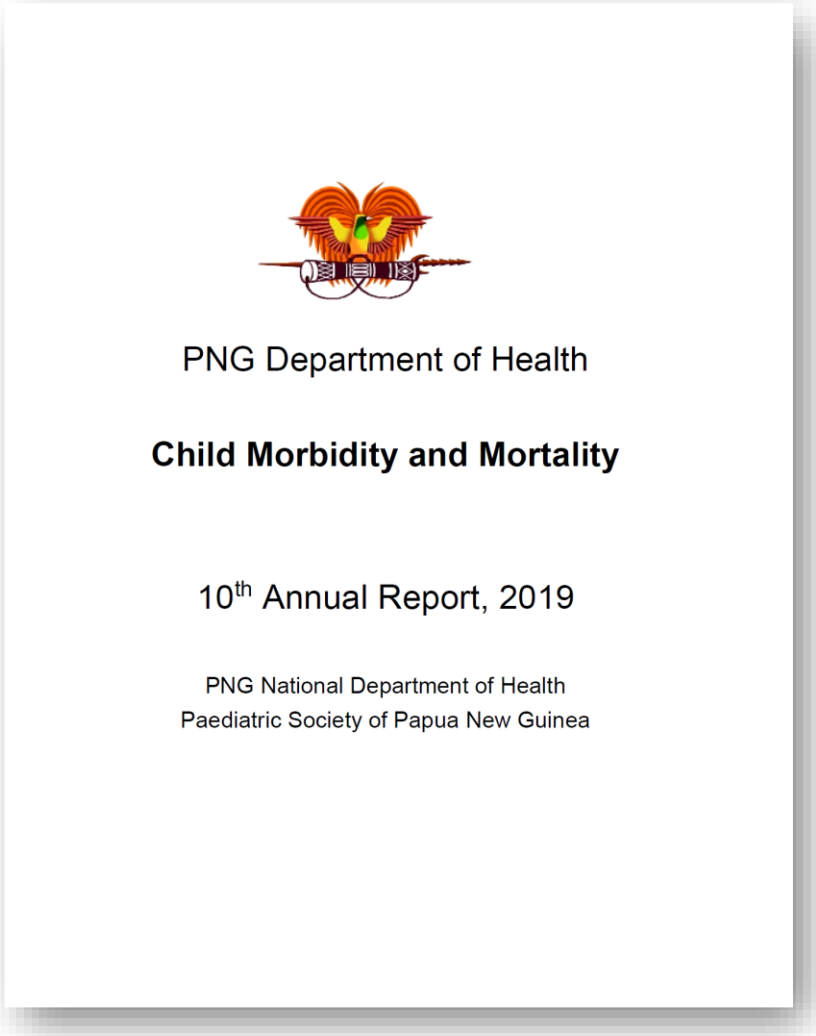
April 26th, 2021

Prof Trevor Duke

- How to detect infections in newborn
- Types and causes of newborn infections
- Focal and systemic infections
- Intrauterine infections (“ToRCHeS”)

Neonatal infections in hospitals

- 58% of neonatal admissions are infections (4624 / 7971), CFR 6%



Increase in sepsis due to multi-resistant enteric gram-negative bacilli in Papua New Guinea

Trevor Duke, Audrey Michael

THE LANCET • Vol 353 • June 26, 1999

Between April 1998 and March 2000, multi-resistant enteric gram negative sepsis occurred in 106 of 5331 paediatric admissions (2%), but caused 87 (25%) of 353 deaths

a	Nosocomial	Community acquired	Chloramphenicol sensitivity	Gentamicin sensitivity
Klebsiella sp*	12	2	0	3
*Pseudomonas aeruginosa**	7	4	0	2
*Escherichia coli**	1	7	1	5
Citrobacter freundii	1	2	1	0
Enterobacter sp	3	4	0	3
Morganella morganii	0	2	2	2
Burkholderia capacia	2	1	1	0
Proteus mirabilis	2	1	0	2
Acinetobacter sp	1	0	0	1
Serratia sp	0	2	0	1
Providentia sp	0	1	1	1
Aeromonas sp	0	1	0	1
Alcaligenes sp	0	1	0	1

*We could not be certain of the origin of one additional isolate of each of these three bacteria.

Sensitivity of bacterial isolates and place of acquisition

Neonatal infections – non-specific symptoms

- **Not feeding well**
- **Drowsy, sleepy or unconscious**
- Fast breathing
- Grunting
- Severe chest indrawing
- Fever >38
- Hypothermia <35.5
- Central cyanosis
- Apnoea
- Severe jaundice
- Severe abdominal distension

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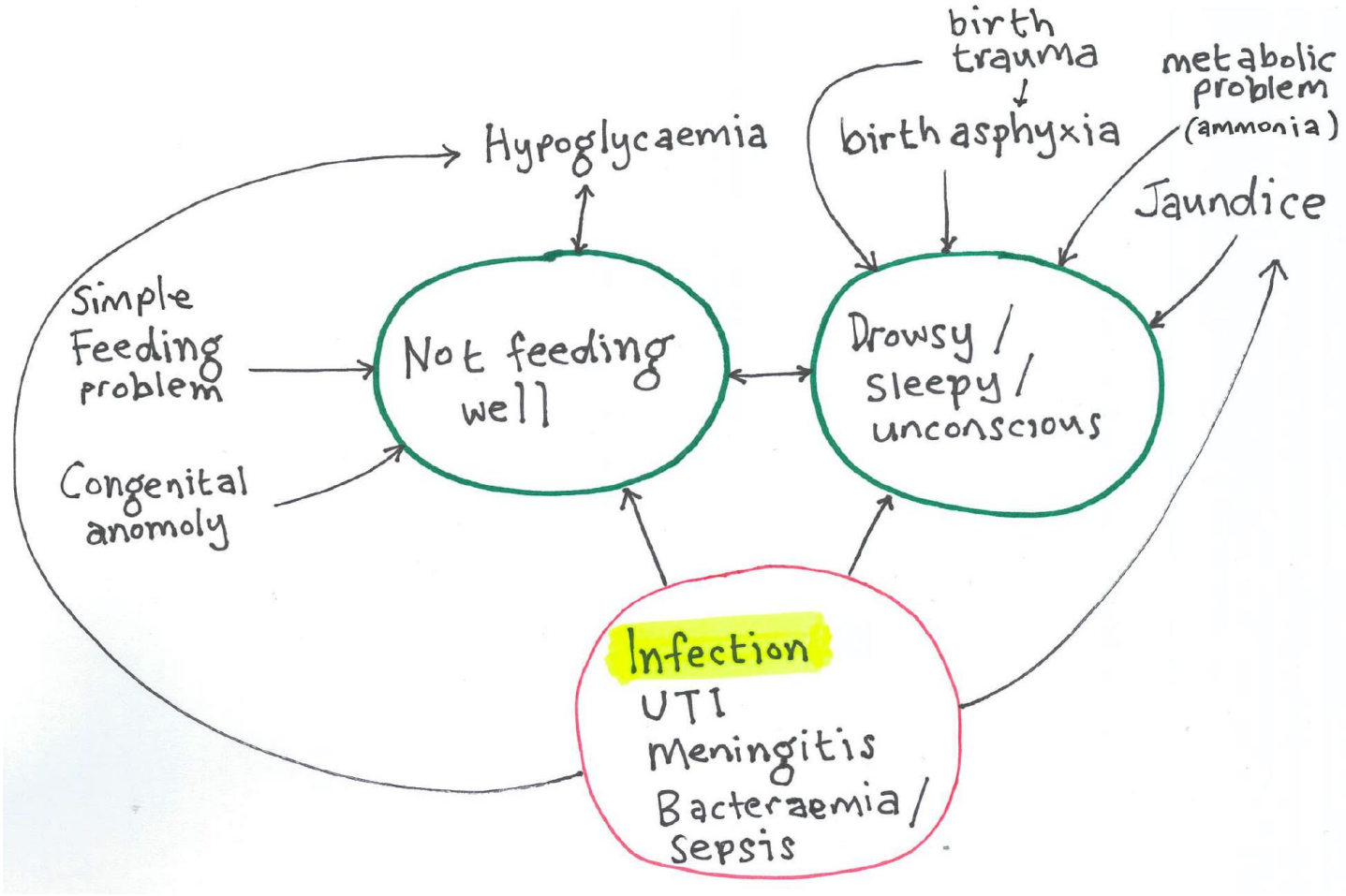
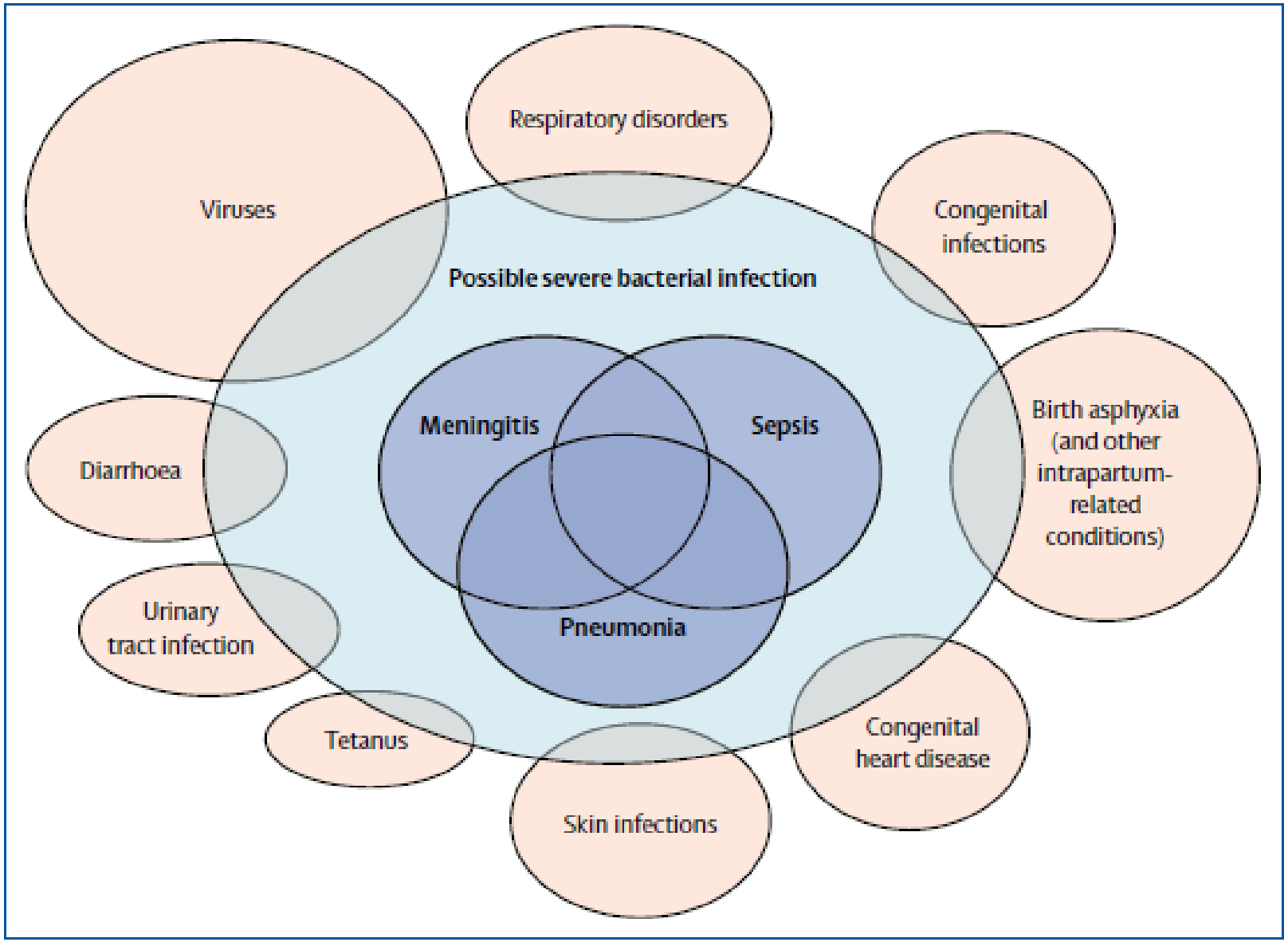




Causes and incidence of community-acquired serious infections among young children in south Asia (ANISA): an observational cohort study
Saha SK, et al. Lancet 2018; 392: 145–59

Neonatal infections

Type of infection

- Pneumonia / bronchiolitis
- Umbilical
- Skin, soft tissue, bone and joint
- Urinary tract infection
- Eye infection
- Diarrhoea
- Bacteraemia / viraemia
- Congenital virus infection

Microbial cause of infection

- Gram positive
  - Staphylococcus aureus
  - Group B streptococcus
- Gram negative
  - E. coli
  - Klebsiella
  - Enterobacter
  - Pseudomonas
- Viral infections
  - Intrauterine
  - RSV, enterovirus, parechovirus
- Congenital TB
- Congenital malaria

Neonatal pneumonia and sepsis

- Early onset sepsis (0-72 hours) – Gram negative bacteria predominantly

Bacteria	Number
E. coli	71
A. aerogenes	45
Streptococcus beta haemolytic	29
P. aeruginosa	27
Streptococcus viridans	21
S. aureus	17
P. vulgaris	11
Streptococcus non haemolytic (Group D)	8

Cultures of lung puncture on 755 neonates who were stillborn or died in the first 72 hours of life

Late onset neonatal sepsis and pneumonia

Bacteria	Number
Total	1313
Total positive cultures	64 (4.9)
Streptococcus pyogenes	14
Staph aureus	15
S. pneumonia	8
E. coli	10
Salmonella spp	8
Group B Streptococcus	2
Klebsiella pneumoniae	2
Enterobacter	2
H. influenzae	1
Group G streptococcus	1
Acinetobacter	1
Pseudomonas	0
Enterococcus spp	0

Skin, umbilical infection with erythema

- Mostly Gram positive – Staph aureus
- Look for the full extent of the infection
  - Is it just skin?
  - Is there an abscess?
  - What compartment is involved?
    - Skin (cellulitis)
    - Fascia (fasciitis)
    - Muscle (pyomyositis)
    - Joints (septic arthritis)
    - Bone (osteomyelitis)
    - Intra-abdominal spread (peritonitis)
  - Is the infant systemically unwell (focal infection or systemic)

Treatment

- Flucloxacillin 50mg/kg Q6 (+ Gentamicin)
- Source control

Purpura (purple spots)

- Gram negative infections
  - E.g. meningococcal disease
  - Pseudomonas

- Ampicillin and gentamicin
- Ceftriaxione / ceftazidime
- Ampicillin and Amikacin

Definition of neonatal *pneumonia*

Respiratory distress (rapid, noisy or difficult breathing, RR>60/min, chest retractions, cough, grunting) who has:
A positive blood culture, or
Any 2 or more of the following:

- **Maternal risk factors**
  - Maternal fever (>38° C)
  - Foul smelling liquor
  - Prolonged rupture of membranes (>24 hours)
- **Clinical picture of sepsis**
  - Poor feeding
  - Lethargy, poor reflexes
  - Hypothermia or hyperthermia
  - Abdominal distension
- **X-ray picture suggestive of pneumonia.** Radiological changes not resolved within 48 hours.
- **Positive sepsis screen**
  - Bands >20% of leucocytes
  - Leucocyte count out of reference range

Neonatal pneumonia treatment

- Oxygen
- Antibiotics

First line

- Ampicillin (Gram positive) and gentamicin (Gram negative)
- Flucloxacillin (Gram positive) and gentamicin (Gram negative), if Staph suspected

Second line

- Amikacin or ciprofloxacin if ESBL suspected (hospitals acquired, proven on blood culture)
- Ceftriaxione no better than Amp and Gent, unless you suspect meningitis

Breast abscess - Staphylococcus

Umbilical abscess - Staph

Staph pustules

Unwell +/-
Fever +/-
Pus draining from lesions

Conditions that are not infections
“Toxic erythema of newborn”

Pustule surrounded by an erythematous halo: lesions usually appear on the second day of life and disappear 5-14 days. Not infectious

Conditions that are not infections: Miliaria

Tiny white spots due to accumulation of sweat in blocked pores.

50% of infants have milia on the face

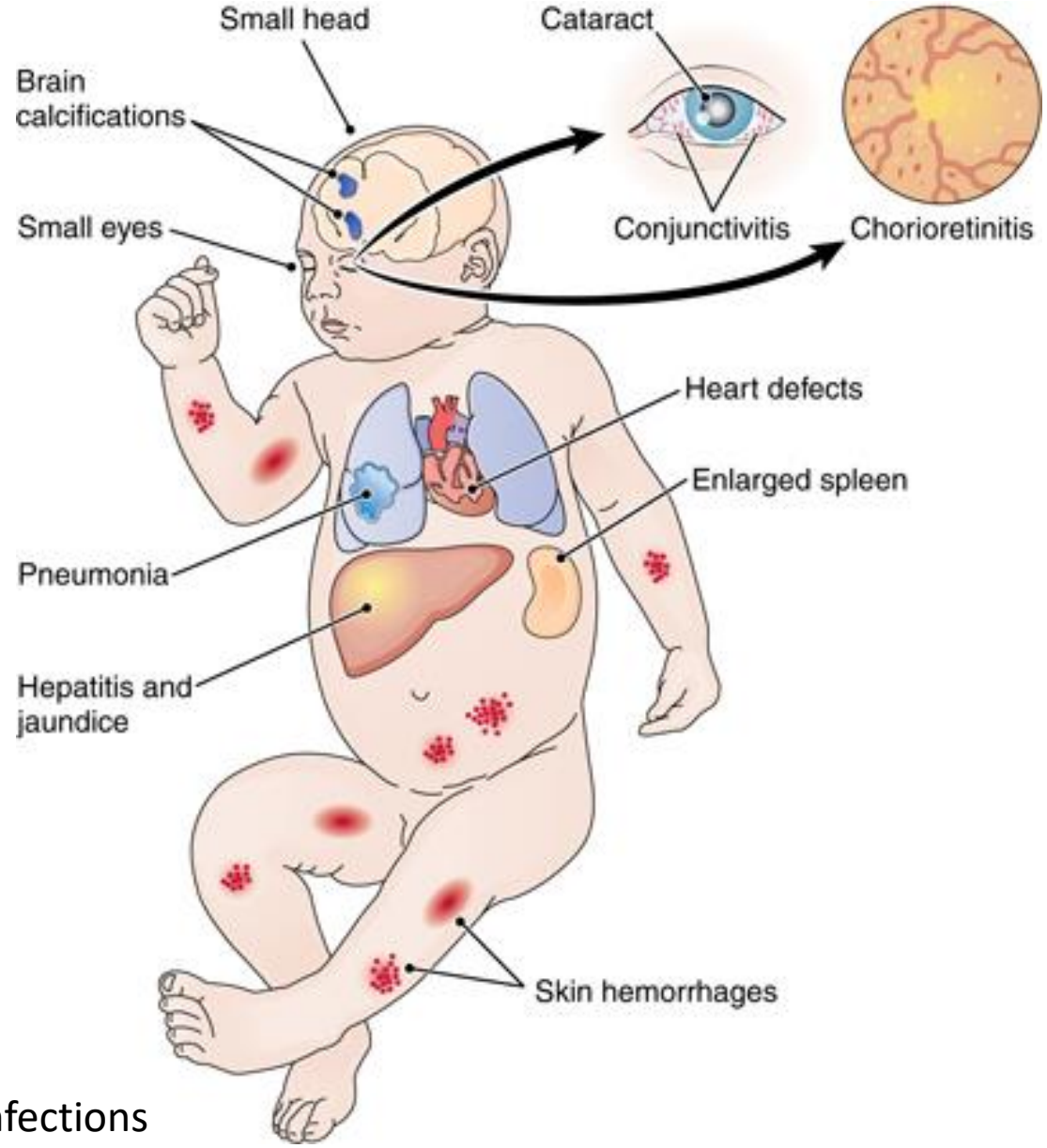
Most resolve in the first 4 weeks of life

Not infectious

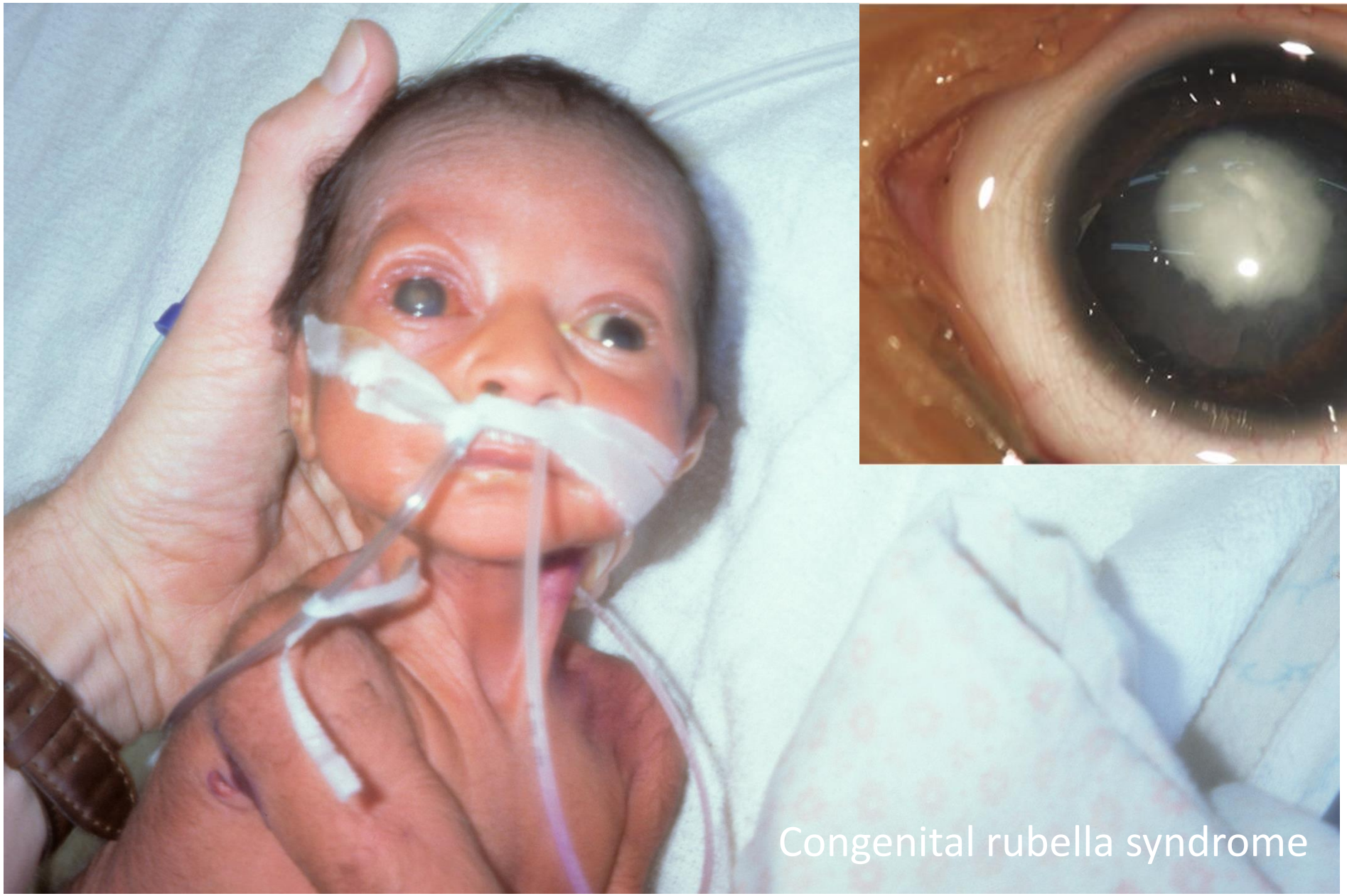
Gonococcal opthalmitis

- Most *N. gonorrhea* resistant to penicillin
- Need ceftriaxone 50mg/kg single IM dose

ToRCHeS infections



step1.medbullets.com/microbiology/104120/torches-infections



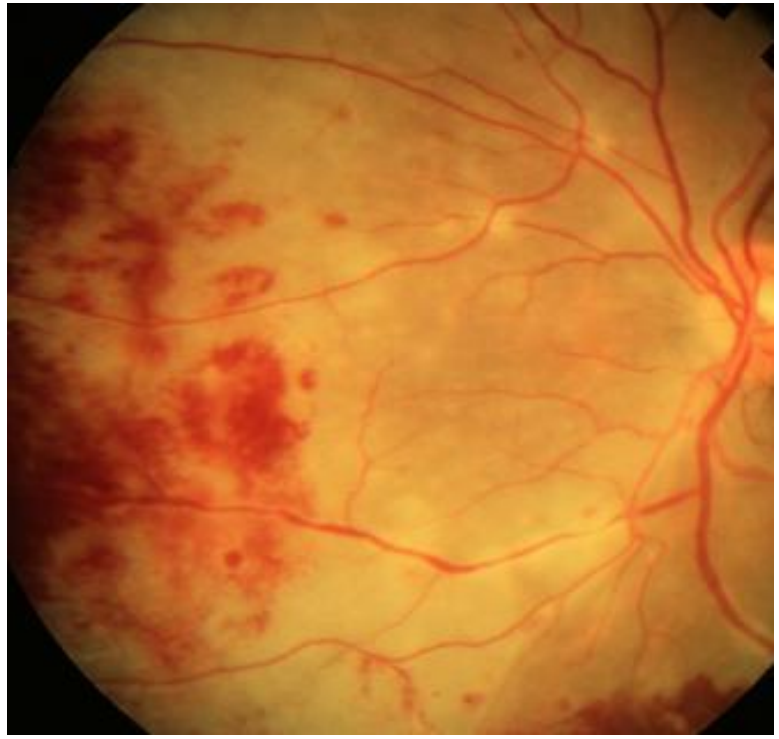
Congenital rubella syndrome

Cytomegalovirus

- Primary infection
  - Glandular fever or flu-like illness
  - Respiratory infection
  - Systemic features – malaise, night sweats, rash, jaundice
- Transmitted in all body fluids (saliva, stool, urine, etc.)
- Highest risk of CRS in fetuses of mothers with primary infection
- Risk still exists for fetuses of mothers with non-primary infection (reactivation or secondary infection with another strain).
- HIV is a risk factor for vertical transmission of CMV (but most CRS is not related to HIV).

Congenital CMV infection

- Most common infective cause of congenital hearing loss.
- Features in neonate
  - Sensory-neural hearing loss
  - Microcephaly
  - Petechiae and thrombocytopenia
  - Chorioretinitis and visual impartment in 22-58% of symptomatic infants

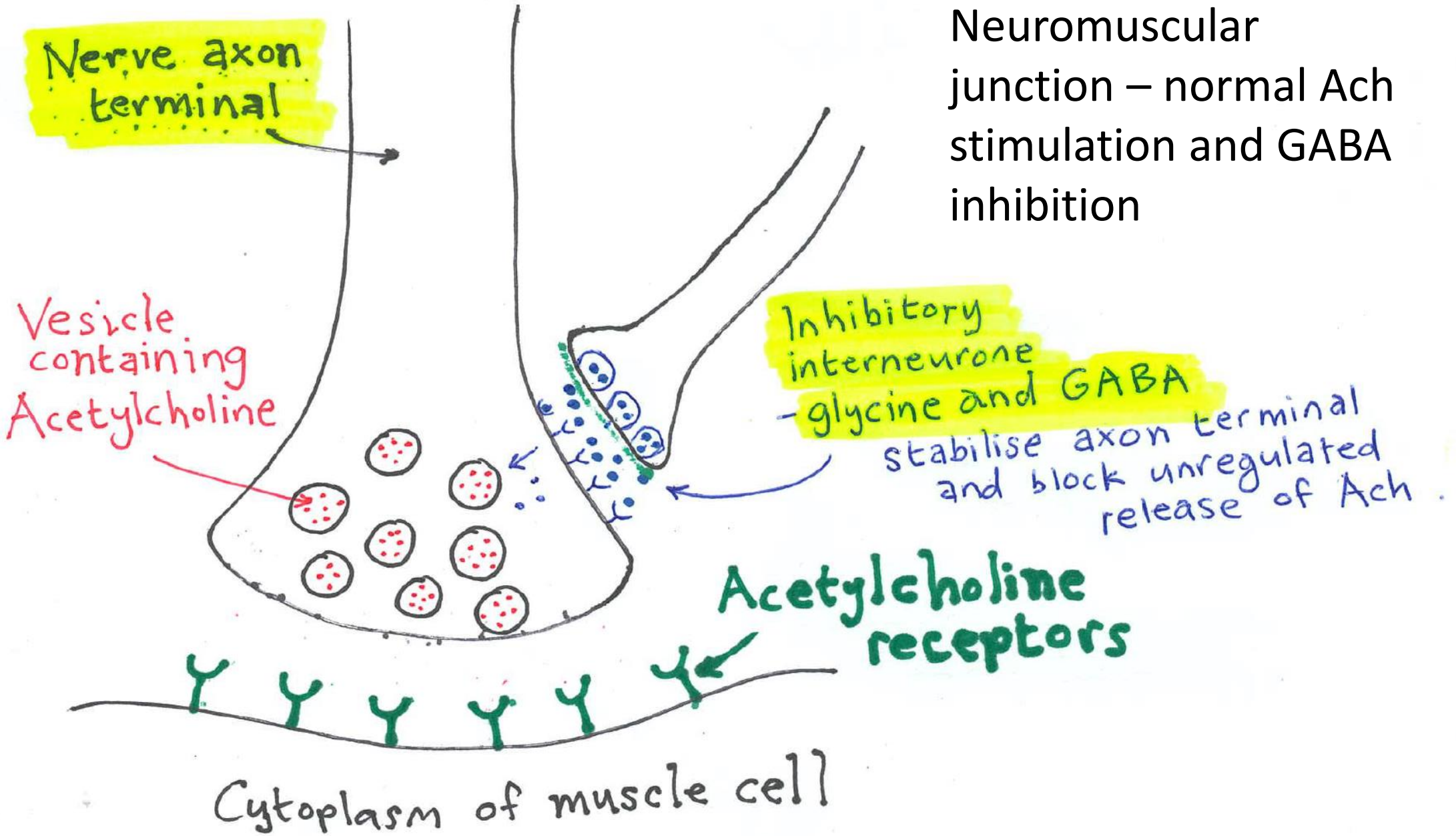


Microcephaly

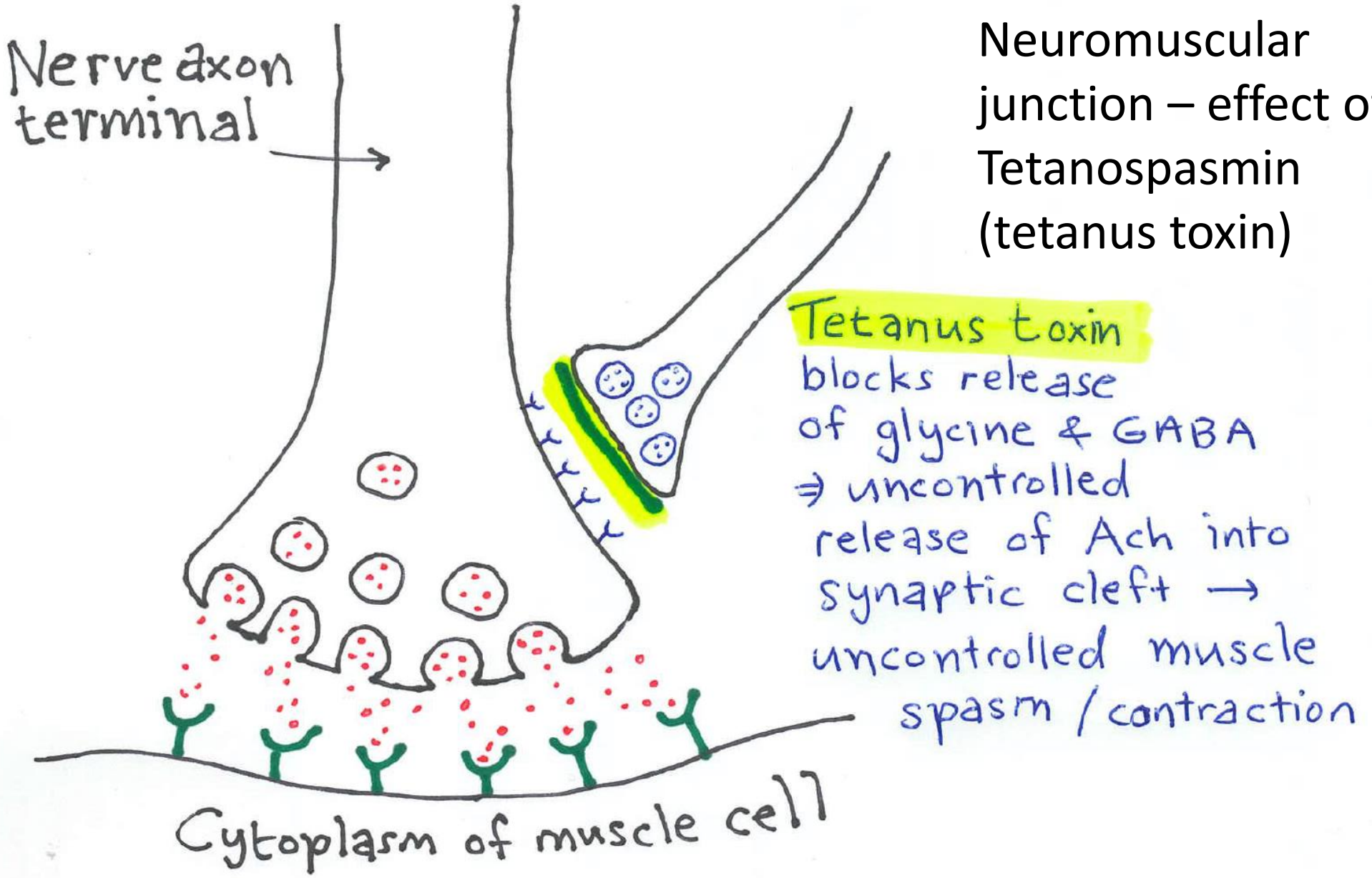
- Intrauterine virus infections
  - Rubella syndrome
    - Cardiac (coarctation of aorta), cataracts, micropthalmia, petechiae
  - Zika virus infection
  - Syphilis
  - CMV
  - Toxoplasmosis
- Genetic / chromosomal
- Toxin exposure
  - Foetal alcohol syndrome (“FASD”: Foetal alcohol spectrum disorder)
  - Drug abuse (cocaine)
  - Mercury poisoning
  - Teratogens, e.g. phenytoin

Neonatal tetanus

Neuromuscular junction – normal Ach stimulation and GABA inhibition



Neuromuscular junction – effect of Tetanospasmin (tetanus toxin)

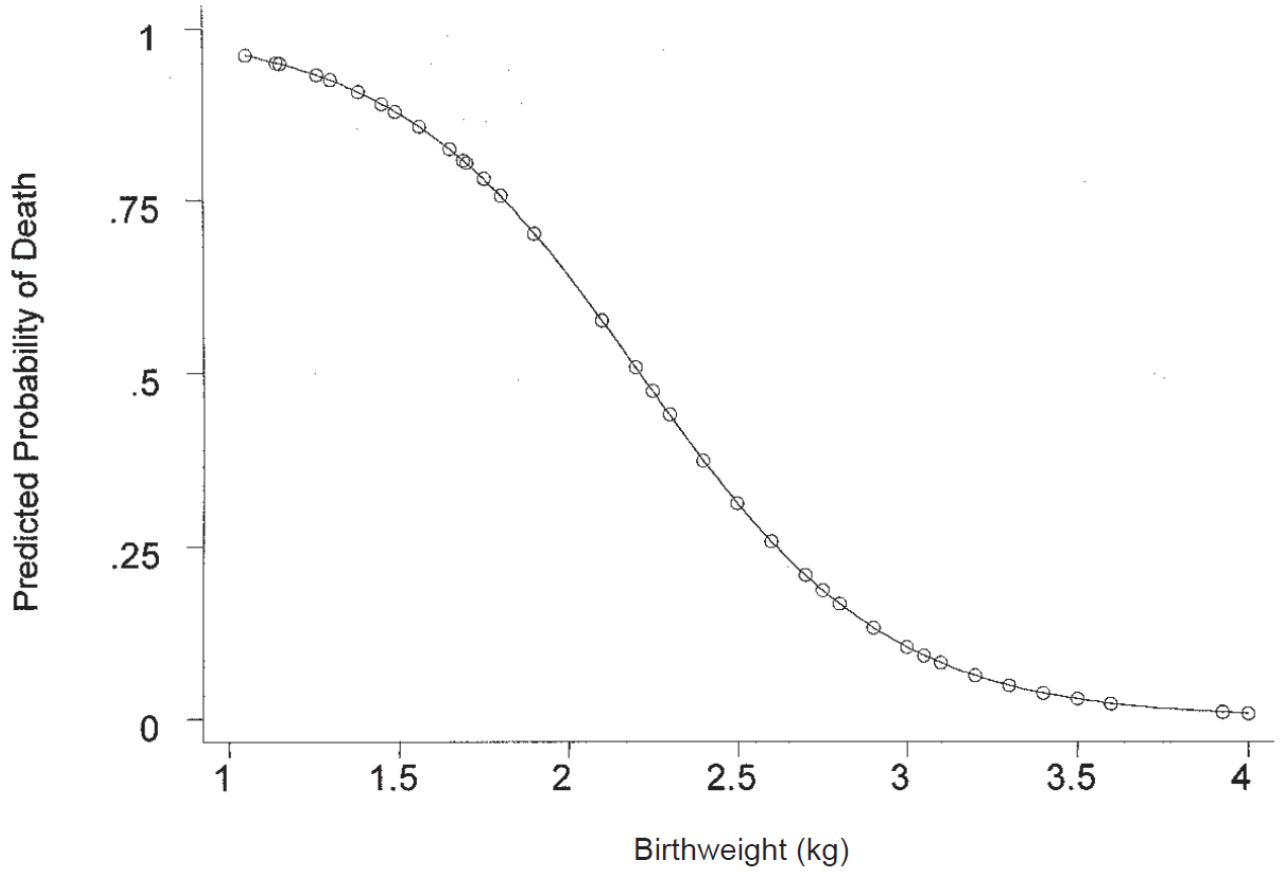


Tetanus treatment

- Avoid all unnecessary handling and noise
- Oxygen
- Paraldehyde 0.2ml/kg
- Diazepam – initially by *slow* IV injection, *not* IM, then orally 0.5mg/kg Q12
- Chlorpromazine – 5mg/kg Q12
- Benzylpenicillin IV Q6 then amoxicillin for total 10 days
- Tetanus immunoglobulin IM (or if you have the IV preparation can be given IT). Give 750 U – 3 amp on admission and 2 amp day 2 and 3
- NG tube feeding
- Autonomic dysfunction (hypertension, tachycardia → hypotension, bradycardia) – $MgSO_4$

Congenital syphilis

- Low birth weight
- Preterm
- Anaemia
- Hepatomegaly
- Splenomegaly
- Ascites
- Jaundice
- Pneumonia
- Periostitis



Congenital syphilis at Goroka Base Hospital: incidence, clinical features and risk factors for mortality

DALE FRANK[1] AND TREVOR DUKE[1,2] PNG Med J 2000 Mar-Jun;43(1-2):121-126

Syphilis treatment

- If asymptomatic (mother VDRL positive)
  - Benzathine penicillin
    - 240,000 U if >2.5kg
    - 120,000 U if <2.5kg
- If symptomatic, preterm or LBW:
  - Benzylpenicillin 50mg/kg BD x 10 days
- Treat the mother

Paediatric Hospital Reporting V12.1

File Edit View Insert Format Records Scripts Window Help

Neonatal Hospital Reporting V12.1

Data entry

Home | Summary data | Export data | Print data form

Pt List | New patient | << | < | ID | > | >>

Patient information | Neonatal conditions

Low birth weight

- ○ >2500 grams
- ○ 1500 - 2500 grams
- ○ 1000 - 1499 grams
- ○ <1000 grams

Prematurity < 37 weeks

○ Yes ○ No

Neonatal infections

- ○ Pneumonia
- ○ Meningitis
- ○ Cord sepsis
- ○ Skin sepsis
- ○ Congenital syphyllis
- ○ Congenital malaria
- ○ Congenital rubella syndrome
- ○ Neonatal tetanus
- ○ Diarrhoea
- ○ Neonatal infection - other
- ○ COVID-19 acute respiratory infection

Neonatal Condtions

- ○ Birth asphyxia / meconium aspiration
- ○ Respiratory distress syndrome(RDS)
- ○ Jaundice
- ○ Bowel obstruction
- ○ Necrotising enterocolitis(NEC)
- ○ Neonatal Other

Congenital Malformations

- ☐ Congenital heart disease
- ☐ Imperforate anus
- ☐ Hirschsprungs disease
- ☐ Malrotation
- ☐ Microcephaly
- ☐ Gastroscisis
- ☐ Ompalocele
- ☐ Congenital genito-urinary malformation
- ☐ Congenital diaphragmatic hernia
- ☐ Congenital lung or airway malformations
- ☐ Spina bifida
- ☐ Congenital limb malformations
- ☐ Congenital abnormalities other

Prevention

- EENC – skin-to-skin contact, early breast feeding, do not separate baby from mother
- Strict hand washing and other basic infection control measures
- Antibiotic stewardship
  - Antibiotics → colonisation of the newborns gastrointestinal tract with pathogenic bacteria that are likely to be invasive (Gram negative, Staph aureus), rather than the protective bacteria that comes from the mother (Lactobacillus, Bifidobacterium).
  - **Avoid antibiotics in babies who do not have serious infections**
  - Cease antibiotics after 24 or 48 hours if the baby is well will also reduce colonisation with pathogenic or highly-resistance bacteria, and reduce infections in babies

FBE markers of bacterial sepsis

↑↑ or ↓↓ WCC
↑↑ or ↓↓ Neutrophils
↑↑ Bands, myelocytes, metamyelocytes
↑↑ Platelets >800,000
↓ Platelets <100,000
↑↑ RDW
“Toxic granulation of neutrophils”

↑↑ Procalcitonin
↑↑ESR